962-94 L-Arginine Improves Exercise Capacity in Patients with Stable Angina

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In patients with ischemic heart disease, endothelial dysfunction may contribute to impaired vasodilation of peripheral and coronary vessels, compromise tissue perfusion and limit exercise capacity. We tested hypothesis that supplementation with L-Arginine improves endothelium-dependent vasodilation with consequent increase in exercise capacity. Twenty two patients with stable angina, mean age 57, on standard medication, randomised to receive L-Arginine orally or placebo were tested with modified Bruce treadmill exercise (ExT) protocol before and after L-Arginine or placebo. ExT variables measured: time to maximum ST depression (s), total ST segment depression (mm), and maximum workload (METS).

ECG ExT variables	L-arginine (n = 12)		p <	Placebo (n = 10)		p <
	before	after		before	after	
Time to maximum depression	500 ± 195	700 ± 173	0.0002	501 ± 101	555 ± 106	0.04
ST segment depression	−6.8 ± 2	−5.5 ± 2	0.04	−6.5 ± 3	−5.4 ± 3	NS
Maximum workload	6.4 ± 2	7.4 ± 3	0.006	5.0 ± 2	5.7 ± 2	NS

Conclusion: L-Arginine improves exercise capacity in patients with stable angina pectoris possibly by increasing nitric oxide synthesis with subsequent improvement in endothelium dependent vascular regulation

962-95 Peripheral Vascular Endothelial Dysfunction in Patients with Microvascular Angina Pectoris

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Previous studies suggest the presence of endothelial dysfunction of coronary microcirculation in patients (pts) with microvascular angina (MVA). To determine whether endothelial dysfunction in MVA is a generalized process we assessed by high ultrasound imaging the change of brachial artery diameter in response to hyperemic flow (endothelium-dependent vasodilator) and to sublingual nitroglycerin (endothelium-independent vasodilator) in 7 women (age 61 ± 7 yrs) with MVA (anginal pain, normal epicardial coronary arteries, positive exercise stress test). Results were compared with 7 age and sex-matched pts with known 3-vessel coronary artery disease (CAD) and 7 age and sex-matched healthy controls. In all subjects intima-media thickness (IMT) of the common carotid artery was measured. Flow-mediated dilatation (FMD) was comparable in MVA and CAD (1.4 ± 2.6% vs 3.7 ± 3.9%, ns); MVA pts had significantly lower FMD compared to controls (1.4 ± 2.6% vs 8.2 ± 2.5%, $p < 0.001$). IMT was significantly lower in pts with MVA compared to CAD (0.63 ± 0.08 mm vs 1.0 ± 0.28 mm, $p < 0.01$) and comparable between MVA and controls (0.63 ± 0.08 mm vs 0.54 ± 0.13 mm, ns); IMT ≥ 0.8 mm was observed in 0/7 MVA pts, 1/7 controls and 7/7 CAD pts. In conclusion, these findings strongly suggest that endothelial dysfunction in MVA is a generalized process involving the peripheral conduit arteries too, and similar to that observed in atherosclerotic disease. IMT could be helpful in discriminating patients with MVA and atherosclerotic CAD.

962-96 Stimulated Hyperinsulinemia in Patients with Microvascular Angina is Associated with Enhanced Red Blood Cell Na^+/Li^+ Countertransport

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Stimulated hyperinsulinemia have previously been found in patients (pts) with microvascular angina (MA). As in pts with hypertension and diabetes insulin resistance is frequently associated with an enhanced activity of red blood cell Na^+/Li^+ countertransport (Na^+/Li^+ CTT, a specific marker of in-vivo sodium-proton antiport activity) the present study was aimed at assessing this pump system in 12 female pts (mean age 57 ± 6 years) with MA and in 10 sex and age-matched controls. Na^+/Li^+ CTT was evaluated as Li^+ efflux from Li^+ loaded eritrocytes. Post-load insulin levels were evaluated by a double-antibody radioimmunoassay. Results are shown in the table.

Test		Controls	MA	p value
Na^+/Li^+ CTT (μmol/L/h)		320|49	642|220	0.0001
Glucose (mg%)	Fasting	76 ± 15	85 ± 7	0.2455
	90 min	95 ± 43	129 ± 47	0.1444
	180 min	74 ± 20	102 ± 39	0.0855
Insulin (μU/ml)	Fasting	10 ± 2	22 ± 23	0.0443
	90 min	41 ± 20	102 ± 73	0.0006
	180 min	16 ± 8	62 ± 46	0.0159

Thus, in patients with MA stimulated hyperinsulinemia is associated with an enhanced activity of the Na^+/Li^+ CTT. The latter may cause microvascular dysfunction through a reduction of intracellular acidosis which, in turn, has the potential to increase the reactivity of smooth muscle cell to constrictor stimuli.

962-114 Environmental Factor is more Important than Angiotensinogen and Angiotensin Converting Enzyme Gene Polymorphism in the Pathogenesis of Coronary Spasm

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This study is to evaluate the role of genetic background of renin angiotensin system in the pathogenesis of vasospasm. Sixty eight patients with coronary vasospasm proved by ergonovine provocation test (M:F = 53:15, mean age: 55.8 yrs) and 48 Patients with normal coronary arteries (M:F = 23:25, mean age: 53.2 yrs) were included in this study prospectively. Angiotensinogen gene polymorphism such as M235T and angiotensin converting enzyme gene polymorphism such as I/D polymorphism were screened and clinical variables were also checked. Allele frequencies of M235 and T235 were 0.61 and 0.39 and I and D were 0.57 and 0.43, respectively, and observed genotype frequencies were in agreement with Hardy-Weinberg equilibrium. On univariate analysis, there were no significant relationship between both types of genetic polymorphisms with coronary vasospasm, except marginal significance of T235 allele frequency and coronary vasospasm ($p = 0.07$). In vasospasm group, there are more male ($p = 0.001$) and smokers ($p = 0.0008$) that were considerably linked to each other. In multivariate analysis male smokers were significantly related to coronary vasospasm (sig T = 0.004) and fasting cholesterol level (sig T = 0.076) and T235 allele of angiotensinogen gene (sig T = 0.1956) did not show statistical significance. *Conclusion:* Environmental factors such as smoking and hypercholesterolemia are more important risk factors of coronary vasospasm than genetic background of renin-angiotensin system.

962-115 Preserved Endothelium Dependent Vasodilatation of Peripheral Circulation in Patients with Variant Angina

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The remarkable correlation of migraine headache, Raynaud's phenomenon and variant angina was reported. This implies that coronary spasm may be a generalized functional abnormality of vasculature. The endothelial dysfunction in patients with effort angina was also demonstrated not only in coronary but in peripheral circulation. However, the endothelial function in peripheral circulation of patient with variant angina is not elucidated. The purpose of this study is to examine the endothelium dependent vasodilatation of patients with variant angina (VAP) in peripheral circulation. We measured the brachial artery diameters at rest (baseline), % increase of diameter during hyperemia (FMD), and that after sublingual nitroglycerin (NTG) in VAP using ultrasonography and compared with those in age-matched patients with effort angina (EAP) and in control subjects (C). The peak flow velocity (FV) was also measured during reactive hyperemia.

	Baseline (mm)	% Increase from baseline		
		FV (%)	FMD (%)	NTG (%)
C (n = 10)	4.6 ± 0.2	282 ± 38	7.6 ± 1.0	16.6 ± 2.5
VAP (n = 12)	4.8 ± 0.1	420 ± 73	8.3 ± 1.3	11.6 ± 1.4
EAP (n = 10)	5.0 ± 0.3	385 ± 40	3.2 ± 0.6*	12.6 ± 1.6

mean ± SEM (*$p < 0.05$, vs. FMD in C, VAP)

There was no difference in nitroglycerin induced vasodilatation among three groups. Flow mediated vasodilatation both in C and VAP was well preserved, but that in EAP was significantly attenuated. These results suggest that endothelium dependent vasodilatation in the peripheral circulation is not impaired in patients with variant angina.

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